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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/697,863	10/30/2003	David E. Clapham	110313.135US3	1595

23483 7590 12/04/2008

WILMERHALE/BOSTON
60 STATE STREET
BOSTON, MA 02109

EXAMINER
WEGERT, SANDRA L

ART UNIT	PAPER NUMBER
1647	

NOTIFICATION DATE	DELIVERY MODE
12/04/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

michael.mathewson@wilmerhale.com
teresa.carvalho@wilmerhale.com
sharon.matthews@wilmerhale.com

Office Action Summary	Application No.	Applicant(s)	
	10/697,863	CLAPHAM ET AL.	
	Examiner	Art Unit	
	SANDRA WEGERT	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6 and 8-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-6, 8-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. This application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid.

Applicants' Remarks and amendments submitted 5 November 2008 are acknowledged. Claims 2, 7 and 26-111 have been cancelled. Claims 1, 3-6 and 8-25 are pending in the instant application.

Claims 1, 3-6 and 8-25 are under examination in the instant Office Action.

Withdrawn Objections/Rejections

Claim Rejections- 35 USC § 102

The following are quotations of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of Claim 8 under 35 U.S.C. 102(b) for being unpatentable over Sanger Centre (1998, Science, 282: 2012-2018, Accession No. Z82256.1) is *withdrawn*. Applicants amended claim 8 so that it no longer recites "a portion" of SEQ ID NO: 1, but rather a fragment

at least "10 consecutive nucleotides." Since the reference teaches a sequence with identical consecutive fragments that are, at most, 8 bases long, the amendment overcomes this particular prior art rejection (5 November 2008).

Claim Rejections - 35 USC § 101 and 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

35 U.S.C. 101 reads as follows:

> **Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.**

The rejection of claims 1, 3-6 and 8-25, under 35 U.S.C. § 101 for lack of Utility is *withdrawn* based on Applicants" arguments (Remarks, 5 November 2008, p. 10). Applicants discussed results from a recent research group that looked at Catsper gene expression in men who had presented to a clinic for non-obstructive azoospermia, or low sperm motility (Nikpoor, et al, 2004, Human Reprod. 19(1): 124-128). In five of the seven men tested, Catsper gene expression was reduced relative to men who had low sperm counts but otherwise normal sperm motility. Nikpoor, et al, measured gene expression of a channel that had the Accession No. AF407333 (see p. 125, under "PCR"), which has 100% sequence homology to SEQ ID NO: 1 of the instant application.

The rejection of claims 1, 3-6 and 8-25, under 35 U.S.C. § 112, first paragraph is *withdrawn in part* based on Applicants' arguments (Remarks, 5 November 2008). Please see the Scope-of-Enablement rejection below.

Maintained/New Objections and/or Rejections

Claim Rejections-35 USC § 112, first paragraph, Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 1, 3-6 and 8-25 are rejected under 35 U.S.C. § 112-1st paragraph, because the specification, while being enabling for the full-length nucleic acid of SEQ ID NO: 1, does not reasonably provide enablement for *variants* or *fragments* of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Applicants are not enabled for *fragments* or *variants* of polynucleotides: 1) at least 10-18 consecutive bases long, 2) identified by substructures of the encoded protein (such as the transmembrane domain, or residues 447-468, etc), 3) having at least 80% sequence identity, or 4) that hybridize to the claimed nucleic acids at low or moderate stringency, as recited in Claims 1, 3-6, 8, 10 and 11, and embraced by claims 1, 3-6 and 8-25.

Applicants' arguments concerning the enablement of variants and fragments of SEQ ID NO: 1 are based on the Utility of the CatSper nucleic acid and also on the probability of specific fragments occurring randomly (Remarks, p. 12). However, even with a now known utility for the full-length SEQ ID NO: 1, applicants have not demonstrated how any fragments or variants

of SEQ ID NO: 1 may be used. All data presented in the instant Specification concern only the full-length nucleic acid of SEQ ID NO: 1. As to the *probability* of a fragment of 10-18 bases of SEQ ID NO: 1 occurring randomly, the examiner agrees that this would be a very unlikely event. However, the probability of random occurrence does not speak to the enablement of short nucleic acids of SEQ ID NO: 1 or of nucleic acids having 80% homology to SEQ ID NO: 1. Perhaps applicants were concerned about the likelihood of whether the nucleic acid fragments could have been randomly disclosed prior to the instant application, about which applicants are directed to the art rejections below.

35 USC § 112, first paragraph - Written Description.

The rejection of Claims 1, 3-6, 8, 10 and 11 under 35 U.S.C. 112, first paragraph- written description- is *maintained.* The reasons for this rejection based on fragments and homology variants of SEQ ID NO: 1 were set forth at pages 5-7 of the previous Office Action (5 August 2008). Applicants did not amend claims referring to non-specific fragments, such as "at least 10 consecutive nucleotides." Applicants also did not cancel language referring to variants identified by substructures of the encoded protein (such as the transmembrane domain of the encoded polypeptide, or residues 447-468), variants having at least "80% sequence identity," or nucleic acids that hybridize to the claimed nucleic acid at moderate stringency. Applicants have neither made nor used *any* variants of SEQ ID NO: 1 or its encoded polypeptide. Therefore applicants were not in possession of all or a significant number of variants of SEQ ID NO: 1 such that a genus is established. Applicants must have invented the subject matter that is claimed and must

be in "possession" of what is claimed (Federal Register, 2001, Vol. 66, No. 4, pages 1099-1111, esp. page 1104, 3rd column).

Applicants argue that one of skill in the art can identify sequences with 80% identity to SEQ ID NO: 1, or to any subsequence thereof (Remarks, p. 14). However, being able to *identify* sequences that are variants or fragments is not the same as being in *possession* of variant sequences at the time of filing. Applicants have not described or shown possession of a commensurate number of species of compounds that are 80% homologous to Catsper1 or are variants of Catsper1. Alternatively, the applicants could have described and used a representative number of species to demonstrate that they are in possession of a genus of Catsper1 variants that function in the same way as SEQ ID NO: 1. However applicants have not demonstrated that they can make any functional fragments or variants belonging to the Catsper1 genus.

Claim Rejections- 35 USC § 102

The following are quotations of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of Claims 10 and 12 under 35 U.S.C. 102(b) for being unpatentable over Sanger Centre (1998, Science, 282: 2012-2018, Accession No. Z82256.1) is *maintained*. The

Sanger Centre Consortium discloses a polynucleotide sequence encoding a nematode sodium channel which is 29% identical to SEQ ID NO: 1 in the instant application. There are several short identical areas where the nucleotides are the same, such as in the region of residues 174-181. This reference meets the limitations of claims 10 and 12 which recite "at least *a portion* of SEQ ID NO: 1," as well as hybridization steps that are not stringent (i.e., washing at 65°C).

Claims 1, 3, 8 and 12 are rejected under 35 U.S.C. 102(b) as being unpatentable over Hillier, et al (1997, Accession No. AA416682.1, see alignment in Appendix A below). Hillier, et al discloses a polynucleotide sequence encoding a calcium channel which is 19.3% identical to SEQ ID NO: 1 in the instant application and 99% identical from residues 1592 to 2056 of SEQ ID NO: 1. This reference sequence meets the limitations of claims 1, 3, 8 and 12 which recite, respectively: at least 10-18 consecutive nucleotides; a sequence encoding a transmembrane loop (specifically the alpha helix as described in the reference); a sequence that hybridizes to at least 10 consecutive nucleotides of SEQ ID NO: 1; and a portion of the nucleic acids described in any of claims 1, 3-6 and 8-11.

Conclusion: Claims 1, 3-6 and 8-25 are rejected for the reasons recited above.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Manjunath Rao, can be reached at (571) 272-0939.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

SLW
26 November 2008

/Elizabeth C. Kemmerer/
Elizabeth C. Kemmerer, Ph.D.
Primary Examiner, Art Unit 1646

APPENDIX A- Search Results

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RESULT 10
AA416682
LOCUS       AA416682                464 bp    mRNA    linear   EST 09-NOV-1997
DEFINITION  zu18d02.r1 Soares_NhHMPu_S1 Homo sapiens cDNA clone IMAGE:738339 5'
            similar to WP:C54D2.5 CE02562 SKELETAL MUSCLE CALCIUM CHANNEL
            ALPHA-1 SUBUNIT ;, mRNA sequence.
ACCESSION   AA416682
VERSION     AA416682.1  GI:2077634
KEYWORDS    EST.
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
            Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 464)
  AUTHORS   Hillier,L., Allen,M., Bowles,L., Dubuque,T., Geisel,G., Jost,S.,
            Krizman,D., Kucaba,T., Lacy,M., Le,N., Lennon,G., Marra,M.,
            Martin,J., Moore,B., Schellenberg,K., Steptoe,M., Tan,F.,
            Theising,B., White,Y., Wylie,T., Waterston,R. and Wilson,R.
  TITLE     WashU-NCI human EST Project
  JOURNAL   Unpublished (1997)
COMMENT     Contact: Wilson RK
            Washington University School of Medicine
            4444 Forest Park Parkway, Box 8501, St. Louis, MO 63108
            Tel: 314 286 1800
            Fax: 314 286 1810
            Email: est@watson.wustl.edu
            This clone is available royalty-free through LLNL ; contact the
            IMAGE Consortium (info@image.llnl.gov) for further information.
            Insert Length: 956   Std Error: 0.00
            Seq primer: -28m13 rev2 ET from Amersham
            High quality sequence stop: 439.
FEATURES             Location/Qualifiers
     source          1. .464
                     /organism="Homo sapiens"
                     /mol_type="mRNA"
                     /db_xref="GDB:5945946"
                     /db_xref="taxon:9606"
                     /clone="IMAGE:738339"
                     /tissue_type="Pooled human melanocyte, fetal heart, and
                     pregnant uterus"
                     /lab_host="DH10B"
                     /clone_lib="Soares_NhHMPu_S1"
                     /note="Organ: mixed (see below); Vector: pT7T3D-PacI;
                     Site_1: Not I; Site_2: Eco RI; Equal amounts of plasmid
                     DNA from three normalized libraries (melanocyte 2NbHM,
                     pregnant uterus NbHPU, and fetal heart NbHH19W) were
                     mixed, and ss circles were made in vitro. Following HAP
                     purification, this DNA was used as tracer in a subtractive
                     hybridization reaction. The driver was PCR-amplified cDNAs
                     from pools of 5,000 clones made from the same 3 libraries.
                     The pools consisted of I.M.A.G.E. clones 260232-265223,
                     340488-345479, and 484488-489479."
ORIGIN

  Query Match             19.3%;  Score 453;  DB 1;  Length 464;
  Best Local Similarity   99.8%;  Pred. No. 1.6e-97;
  Matches  464;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy       1592 CCCACTCCTTCGCCATCTACCACCAAAGCCTCTTCCGGATCCTCAAGGTCTTCAAGAGCC 1651
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 CCCACTCCTTCGCCATCTACCACCAAAGCCTCTTCCGGATCCTCAAGGTCTTCAAGAGCC 60

Qy       1652 TGCGGGCCCTGAGGGCAATCCGGGTCCTGCGGAGGCTCAGCTTCCTGACCAGCGTCCAGG 1711
             ||||||||||||||| ||||||||||||||||||||||||||||||||||||||||||||
Db         61 TGCGGGCCCTGAGGG-AATCCGGGTCCTGCGGAGGCTCAGCTTCCTGACCAGCGTCCAGG 119

Qy       1712 AAGTGACAGGGACCCTGGGCCAGTCCTTGCCGTCCATCGCAGCCATCCTCATCCTCATGT 1771
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        120 AAGTGACAGGGACCCTGGGCCAGTCCTTGCCGTCCATCGCAGCCATCCTCATCCTCATGT 179

Qy       1772 TTACCTGCCTCTTCCTCTTCTCCGCGGTCCTCCGGGCACTGTTCCGCAAATCTGACCCCA 1831
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        180 TTACCTGCCTCTTCCTCTTCTCCGCGGTCCTCCGGGCACTGTTCCGCAAATCTGACCCCA 239

Qy       1832 AGCGCTTCCAGAACATCTTCACCACCATCTTCACCCTCTTCACCTTGCTCACGCTGGATG 1891
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Db        240 AGCGCTTCCAGAACATCTTCACCACCATCTTCACCCTCTTCACCTTGCTCACGCTGGATG 299

Qy       1892 ACTGGTCCCTCATCTACATGGACAGCCGTGCCCAGGGCGCCTGGTACATCATTCCCATCC 1951
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        300 ACTGGTCCCTCATCTACATGGACAGCCGTGCCCAGGGCGCCTGGTACATCATTCCCATCC 359

Qy       1952 TCATAATTTACATCATCATCCAGTACTTCATCTTCCTCAACCTGGTGATTACTGTCCTGG 2011
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        360 TCATAATTTACATCATCATCCAGTACTTCATCTTCCTCAACCTGGTGATTACTGTCCTGG 419

Qy       2012 TGGATAGCTTCCAGACGGCGCTGTTCAAAGGCCTTGAGAAAGCGA 2056
                |||||||||||||||||||||||||||||||||||||||||||
Db        420 TGGATAGCTTCCAGACGGCGCTGTTCAAAGGCCTTGAGAAAGCGA 464
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